STATEMENT OF WORK FOR UNIVERSITY OF PENNSYLVANIA

Title – Restoring Active Memory (RAM): "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)

1.0 SCOPE

This effort promises to use direct brain recordings and stimulation in humans and animals to create a real-time system for enhancing encoding and long-term retrieval of memories for specific types of information. The team consists of nine leading clinical centers for the surgical treatment of epilepsy and movement disorders, each led by a clinician scientist with substantial experience in one or more key areas of electrical brain stimulation, human cognition, computational electrophysiology, and realtime adaptive control systems. The neurological and neurosurgical teams are aligned on the common goal of rapidly developing and testing approaches to enhance and restore memory through a study of unprecedented scope: more than 100 patients each year in a large array of experiments. Pending Investigational Device Exemption (IDE) approval, patients in Phase 2 of the project will be implanted with a complete memory neuromodulation (b)(4) (b)(4) (b)(4) to our memory testing paradigms. This will be accomplished through an accelerated U.S. Food and Drug Administration (FDA) submission of the technical area two (TA2) system at the end of Phase 1. Through application of a computational model of human (b)(4) (b)(4) to the behavioral and electrophysiological data the recipient shall define biomarkers of memory (b)(4) (b)(4). These biomarkers will be used (b)(4) (b)(4) (b)(4) (b)(4) (b)(4).

1.1. BACKGROUND

The Defense Advanded Research Project Agency (DARPA) seeks new methods for analysis and decoding of neural signals in order to understand how neural stimulation could be applied to facilitate recovery of memory encoding following brain injury. Ultimately, it is desired that a prototype implantable neural device that enables recovery of memory in a human clinical population be developed. Additionally, the program encompasses the development of quantitative models of complex, hierarchical memories and exploration of neurobiological and behavioral distinctions between memory function using the implantable device versus natural learning and training.

2.0 APPLICABLE DOCUMENTS

(a) DARPA BAA-14-08.

(b) UPENN Technical Proposal Titled "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)" dated January 23, 2014

3.0 PROJECT WORK DESCRIPTION AND REQUIREMENTS

The recipient shall provide the facilities necessary to develop the effort as described herein.

Human use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Review Board (IRB) approvals, show proper assurance documentation, and obtain proper approval from the Government officials prior to human use testing.

Animal use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Animal Care and Utilization Committee (IACUC) approval and demonstrate this approval to the Government prior to beginning experimentation with animals. If animal use is no longer anticipated, or changes significantly from the approved

IACUC then the PI must submit a letter stating the discontinuation of animal use for this effort and/or receive appropriate authorization for IACUC changes of previously specified protocols. Unless prior approval by DARPA is given IACUC documentation must be provided prior to contract award.

3.1 BASE PERIOD (PHASE I)

Technical Area 1

3.1.1 A computational model for describing behavior in declarative memory tasks.

3.1.1.1 Predicting moment-by-moment behavior in a variety of memory tasks.
The recipient shall document a model of memory (b)(4) (b)(4) (b)(4) (b)(4).

(a) The recipient shall document the code base for the (b)(4) (b)(4) (b)(4) [Month 3].

(b) The recipient shall extend the model (b)(4) (b)(4) [Month 6].

(c) The recipient shall document fully commented, optimized (b)(4) (b)(4) (b)(4) Code shall be able to execute model (b)(4) (b)(4) (b)(4) [Month 6].

(d) The recipient shall document the code base for the (b)(4) (b)(4) (b)(4) [Month 9].

(e) The recipient shall fit the (b)(4) (b)(4) [Month 12].

(f) The recipient shall document fully commented, optimized (b)(4) (b)(4) (b)(4). Code shall be able to execute model (b)(4) [Month 12].

3.1.1.2 The recipient shall close the loop on learning by documenting the model (b)(4) using the same framework (b)(4).

(a) The recipient shall simulate the development of (b)(4) (b)(4) (b)(4). At this milestone the model will be able to simulate (b)(4) (b)(4) [Month 18].

(b) The recipient shall complete the modeling of (b)(4) memory, (b)(4) (b)(4) [Month 24].

(c) The recipient shall document a novel means of estimating (b)(4) This task does not depend on completion of other tasks [Month 24].

3.1.2 Integrating neurophysiological biomarkers into the computational model of behavior.

3.1.2.1 Biomarkers for the encoding and recovery (b)(4)

3.1.2.1.1 A prototype for analyzing (b)(4) neural (b)(4) (b)(4) shall be deployed and evaluated.

3.1.2.1.2 The recipient shall document the prototype software (b)(4) [Month 12].

3.1.2.1.3 Analysis (b)(4) generated from animal data in TA3 shall be accomplished to identify biomarkers (b)(4) and develop algorithms (b)(4) (b)(4). The recipient shall analyze biomarkers (b)(4) from non-human primate neurophysiological data [Month 18].

3.1.2.1.4 The recipient shall document the prototype software (b)(4) This task will be dependent on neurophysiological data collected from patients and also non-human primates. The recipient shall document the software (b)(4) Month 24].

3.1.3 Electrophysiological recordings to define biomarkers (b)(4) (b)(4) memory.

Objective: Define biomarkers of (b)(4) memories, as measured in a broad array of tasks.

The subtask list that follows references the following experiments: (b)(4) free recall of (b)(4) word lists (FR), (b)(4) free recall (b)(4)FR), spatial navigation (b)(4) (b)(4), and paired associate learning (PAL).

3.1.3.1 The recipient shall design, program, pilot, execute, and analyze data from Experiment FR1 on patients in the epilepsy monitoring unit. Recording neural activity (b)(4) shall be used to identify (b)(4) biomarkers (b)(4) of (b)(4) memory (b)(4). These biomarkers will serve a critical role in subsequent (b)(4) experiments. The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 13 patients from experiment FR1 [Month 8].
(d) Analyze data on 26 patients from experiment FR1 [Month 13].
(e) Analyze data on 39 patients from experiment FR1 [Month 18].
(f) Analyze data on 52 patients from experiment FR1 [Month 24].
(g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (neuroradiology) and carry out 3D reconstructions (b)(4) [Month 24].
(h) Complete interim reports on data from the above experiment to be presented at team meetings and with DARPA program personnel. Reports shall include detailed analyses of behavioral data, (b)(4) (b)(4) as well as analyses of the electrophysiological correlates of (b)(4) memory (b)(4) (b)(4) [Month 24].
(i) Post all data collected in a deidentified format compatible with the public IEEG data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.3.2 Design, program, pilot, execute, and analyze data from Experiment CatFR1 (n=46) on patients in the epilepsy monitoring unit.

In this task the recipient shall define biomarkers of (b)(4) (b)(4) (b)(4) (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 11 patients from experiment CatFR1 [Month 8].
(d) Analyze data on 23 patients from experiment CatFR1 [Month 13].
(e) Analyze data on 34 patients from experiment CatFR1 [Month 18].
(f) Analyze data on 46 patients from experiment CatFR1 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete interim reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.3.3 Design, program, pilot, execute, and analyze data from Experiment YC1 (n=44) on patients in the epilepsy monitoring unit.
In this task the recipient shall identify biomarkers of (b)(4) memory (b)(4) . (b)(4) (b)(4) (b)(4) The recipient shall identify (b)(4) memory biomarkers, (b)(4) , as well as (b)(4) memory biomarkers, (b)(4) .
The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3]
(c) Analyze data on 11 patients from experiment YC1 [Month 8].
(d) Analyze data on 22 patients from experiment YC1 [Month 13].
(e) Analyze data on 33 patients from experiment YC1 [Month 18].
(f) Analyze data on 44 patients from experiment YC1 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete interim reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.3.4 Design, program, pilot, execute, and analyze data from Experiment PAL1 (n=30) on patients in the epilepsy monitoring unit. In this task the recipient shall identify biomarkers (b)(4) of (b)(4) associations and shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 7 patients from experiment PAL1 [Month 8].
(d) Analyze data on 14 patients from experiment PAL1 [Month 13].
(e) Analyze data on 22 patients from experiment PAL1 [Month 18].
(f) Analyze data on 30 patients from experiment PAL1 [Month 24].

(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete interim reports on data from the above experiment [(Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reportin on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.3.5 Design, program, pilot, execute and analyze data from Experiment DBS2 (n=20) on patients undergoing DBS for movement disorders and Parkinson's Disease. In this task the recipient shall perform a (b)(4) recall task (see (b)(4) Recall Task, above). (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 5 patients from experiment DBS2 [Month 8].
(d) Analyze data on 10 patients from experiment DBS2 [Month 13].
(e) Analyze data on 15 patients from experiment DBS2 [Month 18].
(f) Analyze data on 20 patients from experiment DBS2 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete interim reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4 Stimulation to (b)(4) (b)(4) memory

3.1.4.1 Design, program, pilot, execute, and analyze data from Experiment FR2 (n=18). The recipient shall test the hypothesis (b)(4) . The recipient shall compare the degree to which (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 4 patients from experiment FR2 [Month 8].
(d) Analyze data on 8 patients from experiment FR2 [Month 13].
(e) Analyze data on 13 patients from experiment FR2 [Month 18].
(f) Analyze data on 18 patients from experiment FR2 [Month 24].
(g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (neuroradiology) and carry out 3D reconstructions (b)(4) [Month 24].
(h) Complete final reports on data from the above experiment to be presented at team meetings and with DARPA program personnel. Reports shall include detailed analyses of behavioral data, (b)(4) (b)(4) , as well as analyses of the electrophysiological

correlates of (b)(4) memory (b)(4) [Month 24].

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.2 Design, program, pilot, execute, and analyze data from Experiment FR3 (n=18). The recipient shall test (b)(4) and shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 4 patients from experiment FR3 [Month 8].
(d) Analyze data on 8 patients from experiment FR3 [Month 13].
(e) Analyze data on 13 patients from experiment FR3 [Month 18].
(f) Analyze data on 18 patients from experiment FR3 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.3 Design, program, pilot, execute, and analyze data from Experiment FR7 (n=3). In experiment FR7 the recipient (b)(4) shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 1 patient from experiment FR7 [Month 12].
(d) Analyze data on 2 patients from experiment FR7 [Month 18].
(e) Analyze data on 3 patients from experiment FR7 [Month 24].
(f) Organize and annotate patient data from above experiment [Month 24].
(g) Complete interim reports on data from the above experiment [Month 24].
(h) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(i) Fully document code for experiment [Month 2].
(j) Fully document analysis functions [Month 3].
(k) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(l) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(m) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.4 Design, program, pilot, execute, and analyze data from Experiment CatFR2. (b)(4). Further, the recipient (b)(4) shall:

(a) Design, program, and pilot task [Month 2].

(b) Write initial data analysis scripts [Month 3].
(c) Analyz data on 4 patients from experiment CatFR2 [Month 8].
(d) Analyze data on 8 patients from experiment CatFR2 [Month 13].
(e) Analyze data on 13 patients from experiment CatFR2 [Month 18].
(f) Analyze data on 18 patients from experiment CatFR2 [Month 24].
(g) Organize and annotate patient data from above [Month 24].
(h) Complete final reports on data from the above experiment [Month 24]
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.5 Design, program, pilot, execute, and analyze data from Experiment CatFR3. In CatFR3 the recipient shall test the ability of (b)(4) stimulation (b)(4) to enhance memory (b)(4) (b)(4) (b)(4) (b)(4) (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyz data on 4 patients from experiment CatFR3 [Month 8].
(d) Analyz data on 8 patients from experiment CatFR3 [Month 13].
(e) Analyz data on 13 patients from experiment CatFR3 [Month 18].
(f) Analyz data on 18 patients from experiment CatFR3 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.6 Design, program, pilot, execute, and analyze data from Experiment YC2. Therecipient shall apply (b)(4) stimulation (b)(4) (b)(4). The recipient shall test the ability of stimulation to improve memory (b)(4) . The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 5 patients from experiment YC2 [Month 8].
(d) Analyz data on 10 patients from experiment YC2 [Month 13].
(e) Analyz data on 16 patients from experiment YC2 [Month 18].
(f) Analyz data on 22 patients from experiment YC2 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]
(n) Post annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.7 Design, program, pilot, execute, and analyze data from Experiment YC3. (b)(4) (b)(4) the recipient shall assess the (b)(4) to significantly (b)(4) (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 5 patients from experiment YC3 [Month 8].
(d) Analyze data on 10 patients from experiment YC3 [Month 13].
(e) Analyze data on 16 patients from experiment YC3 [Month 18].
(f) Analyze data on 22 patients from experiment YC3 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 (Month 24)
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.8 Design, program, pilot, execute, and analyze data from Experiment PAL2. (b)(4) The recipient (b)(4) shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 3 patients from experiment PAL2 [Month 8].
(d) Analyze data on 6 patients from experiment PAL2 [Month 13].
(e) Analyze data on 9 patients from experiment PAL2 [Month 18].
(f) Analyze data on 12 patients from experiment PAL2 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Profide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.9 Design, program, pilot, execute, and analyze data from Experiment PAL3. (b)(4) (b)(4)

The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 3 patients from experiment PAL3 [Month 8].
(d) Analyze data on 6 patients from experiment PAL3 [Month 13].
(e) Analyze data on 9 patients from experiment PAL3 [Month 18].
(f) Analyze data on 12 patients from experiment PAL3 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.4.10 Design, program, pilot, execute and analyze data from Experiment DBS1.
The recipient shall evaluate (b)(4) for (b)(4) learning during a (b)(4) task. (b)(4) (b)(4) The recipient shall vary (b)(4) parameters. (b)(4) The recipient shall index learning (b)(4) (b)(4) The recipient shall compare (b)(4) across the five conditions (b)(4) , and (2) identify (b)(4) parameters (b)(4) and shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 12 patients from experiment DBS1 [Month 8].
(d) Analyze data on 24 patients from experiment DBS1 [Month 13].
(e) Analyze data on 36 patients from experiment DBS1 [Month 18].
(f) Analyze data on 48 patients from experiment DBS1 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete interim reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

3.1.5 Stimulation (b)(4) in (b)(4) patients with implanted (b)(4) devices
In the following tasks the recipient shall seek (b)(4) patients implanted with (b)(4) devices by recruiting patients (b)(4) and assess the effects of stimulation on performance (b)(4) .

3.1.5.1 Design, program, pilot, execute, and analyze data from Experiment NP1 (b)(4) (b)(4) Behavioral and stimulation methods shall follow the design of experiment FR2 [Months 1–12].
The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].

(c) Analyze data on 5 patients from experiment NP1 [Month 6].
(d) Analyze data on 10 patients from experiment NP1 [Month 12].
(e) Complete final reports on data from the above experiment to be presented at team meetings and with DARPA program personnel. Reports shall include detailed analyses of behavioral data, (b)(4) (b)(4) as well as analyses of the electrophysiological correlates of (b)(4) memory (b)(4) [Month 24].
(f) Post all data collected so far in a deidentified format compatible with the public data portal [Month 12].
(g) Fully document code for experiment [Month 2].
(h) Fully document analysis functions [Month 3].
(i) Create 3D reconstructions of all patients run in the task [Month 12].
(j) Provide final reporting on analyzed data from all patients run in the task [Month 12].
(k) Post fully annotated data posted to the public data portal for all patients run in the task [Month 12].

3.1.5.2 Develop algorithms (b)(4) . The recipient shall:
(a) Complete 6-month interim report (b)(4) , (b)(4) [Month 6].
(b) Develop prototype (b)(4) (b)(4) (b)(4) . Complete 12-month interim report on algorithms [Month 12].
(c) Develop refined version of prototype (b)(4) (b)(4) (b)(4) Complete 18-month interim report on algorithms [Month 18].
(d) Finalize (b)(4) algorithms (b)(4) (b)(4) Complete final report on algorithms [Month 24].
(e) Provide 6-month interim report on (b)(4) algorithms [Month 6].
(f) Provide 12-month interim report on (b)(4) algorithms [Month 12].
(g) Document 12-month prototype (b)(4) algorithms [Month 12] .
(h) Provide 18-month interim report on (b)(4) algorithms [Month 18].
(i) Document 18-month refined prototype (b)(4) algorithms [Month 18].
(j) Provide final reporting on (b)(4) algorithms [Month 24].
(k) Document finalized (b)(4) algorithms [Month 24].

3.1.1.5.3 Design, program, pilot, execute, and analyze data from NP2 (b)(4) [Months 13–24]. The recipient shall:
(a) Design, pilot, and program task [Month 14].
(b) Write initial data analysis scripts [Month 15].
(c) Analyze data on 5 patients from experiment NP2 [Month 20].
(d) Analyze data on 10 patients from experiment NP2 [Month 24].
(e) Complete final reports on data from the above experiment [Month 24].
(f) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(g) Fully document code for experiment [Month 14].
(h) Fully document analysis functions [Month 15].
(i) Create 3D reconstructions of all patients run in the task [Month 24].
(j) Provide final reporting on analyzed data from all patients run in the task [Month 24].
(k) Post fully annotated data to the public data portal for all patients run in the task [Month 24].

3.1.5.4 Design, program, pilot, execute, and analyze data from NP3 [Months 13–24]. The recipient shall:

(a) Design, pilot, and program task [Month 14].
(b) Write initial data analysis scripts [Month 15].
(c) Analyze data on 5 patients from experiment NP3 [Month 20].
(d) Analyze data on 10 patients from experiment NP3 [Month 24].
(e) Complete final reports on data from the above [Month 24].
(f) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(g) Fully document code for experiment [Month 14].
(h) Fully document analysis functions [Month 15].
(i) Create 3D reconstructions of all patients run in the task [Month 24].
(j) Provide final reporting on analyzed data from all patients run in the task [Month 24].
(k) Post fully annotated data to the public data portal for all patients run in the task [Month 24].

3.1.6 Core project resources devoted to TA1.

3.1.6.1 The recipient shall perform electrophysiological experiment development and programming, data analysis, computational cluster effort towards data analysis and computational modeling fr TA1.

3.1.6.2 The recipient shall provide project coordination, data sharing and data storage.

3.1.7 Determine electrode requirements for (b)(4) stimulation in Phase 2. The recipient shall characterize (b)(4) for modulating and restoring memory function.

3.1.7.1 The recipient shall determine whether FDA-approved, commercial electrodes (b)(4) are capable (b)(4) The recipient shall:
(a) Based on precise anatomical analyses (b)(4) [Month 12].
(b) Working with commercial electrode manufacturers, determine optimal design with current technology that can be put into place by the beginning of Phase 2 [Month 12].
(c) Use modified electrodes in a minimum of 10 patients to be studied in Months 19–24 [Month 18].
(d) Analyze and report to DARPA on enhanced efficacy of (b)(4) electrodes in support of proposed study in Phase 2.

3.1.8 The recipient shall provide TA1 electrophysiological experiment development and programming, data analysis, computational cluster effort towards data analysis and computational modeling.

3.1.9 The recipient shall provide project coordination, data sharing, data storage

Technical Area 2

3.1.10 Validate system architecture and individual The recipient shall document and review the high-level system design requirements against current design assumptions.

3.1.10.1 The recipient shall validate system level specification with TA1 team [Months 1–3].

3.1.10.2 The recipient shall continue to refine parameters for neural interfaces [Months 1–6].

3.1.10.3 The recipient shall refine the specifications for electronics (b)(4) continually refining as needed [Months 4–6].

3.1.10.4 The recipient shall validate the specification for the Algorithm prototyping system and user interface [Months 5–6].

3.1.10.5 The recipient shall define the sub-chronic safety and performance data required by the FDA for 29-day IDE approval [Month 6] and shall:

(a) Document definitions of the functional, operation, and performance requirements of the overall system [Month 3] .

(b) Document definitions of the component-level specifications for the neural interface, electronics, external packaging, and algorithm prototyping system [Month 6].

(c) Document definitions of the sub-chronic safety and performance data required by the FDA for the 29-day IDE approval [Month 6]

3.1.11 Design, fabrication, and characterization of the external neuromodulation stimulator The recipient shall develop (b)(4) interfaces with (b)(4) electrodes.

3.1.11.1 The recipient shall design and manufacture of electronics, (b)(4) [Months 7–18].

3.1.11.2 The recipient shall embedd software (firmware) to control the electronics and provide (b)(4) capability [Months 7–18].

3.1.11.3 The recipient shall modify design and manufacture the mechanical connector (b)(4) to interface with the clinical depth electrodes and cortical/subcortical grids/strips [(Months 7–18].

3.1.11.4 The recipient shall manufacture, test, document safety and performance testing, and deliver (b)(4) in preparation for FDA IDE submission and system delivery to clinical sites [Months 19–24].

(a) Design and build electronics, (b)(4) [Months 7-18].

(b) Document the (b)(4) software that controls the electronics and document (b)(4) algorithm capability [Month 18].

(c) Modify the design of the mechanical connector and build 40 (b)(4) to interface with electrodes [Month18].

(d) Test and document safety and performance (b)(4) in preparation for FDA IDE submission [Month 24].

3.1.12 Connectorization and Integration of electrode arrays with (b)(4) (b)(4) stimulator. The recipient shall develop a connectorization method and integrate a variety of clinical electrode designs with the Medtronic (b)(4) neural stimulator.

3.1.12.1 The recipient shall define specifications for the connector (b)(4) [Months 1–3].

3.1.12.2 The recipient shall design and fabricate the medical grade ceramics, both the male version for the (b)(4) interface and the female version (b)(4) [Months 3–9].

3.1.12.3 The recipient shall document the assembly process (b)(4) [Months 9–15].

3.1.12.4 The recipient shall design verification testing to ensure electrical conductivity and reliability, moisture resistance, mechanical integrity [Months 15–24]. The recipient shall:

(a) Define specifications for the connector [Month 3].
(b) Design and fabricate medical grade ceramic [Month 9].
(c) Document the assembly process (b)(4) [Month 15].
(d) Complete and document connector Prototype [Month 15].
(e) Design verification testing to ensure electrical conductivity and reliability, moisture resistance, mechanical integrity [Month 24].

3.1.13 Algorithm prototyping system. The recipient shall develop an algorithm prototyping system (b)(4).

3.1.13.1 The recipient shall design (b)(4) interface (b)(4) [Months 1–6].

3.1.13.2 The recipient shall document the software used (b)(4) [Months 1–12].

3.1.13.3 The recipient shall develop software (b)(4) [Months 7–18].

3.1.13.4 The recipient shall verify and validate testing and documentation for IDE submission [Months 19–24]. The recipient shall:

(a) Design (b)(4) interface (b)(4) [Month 6].
(b) Document the software used (b)(4) [Month 12].
(c) Document the software (b)(4) [Month 18].
(d) Complete prototype software package [Month 18].
(e) Verifiy and validatr testing and documentation for IDE submission [Month 24].

3.1.14 System verification and validation testing. The recipient shall evaluate and verify system lifetime, sterility and biocompatibility. The recipient shall also verify and validate the system functions and interfaces (b)(4) (b)(4) Additionally, system verification and validation shall be performed.

3.1.14.1 Lifetime testing: The recipient shall fully-integrated systems (b)(4). The device shall be interrogated at specific time-intervals to study any degradation or failures of the neural interfaces and connectors [Months 13–18].

3.1.14.2 The recipient shall perform sterility testing as outlined in ANSI / AAMI / ISO 11135-1:2007 [Months 19–24].

3.1.14.3 The recipient shall perform biocompatibility testing for sub-chronic (< 29-days) implantation as outlined in ANSI / AAMI / ISO 10993-3:2008 for the neural interfaces [Months 19–24].

3.1.14.4 The recipient shall perform (b)(4) system verification testing for sub-chronic (< 29-days) implantation as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Months 19–24].

3.1.14.5 The recipient shall perform surgical procedure validation via acute animal testing [Month 19–24]. The recipient shall:

(a) Fabricate and assemble fully-integrated systems for testing [Month 18].
(b) Report on accelerated lifetime testing of the fully-integrated system to study any degradation or failures of the neural interfaces and connectors [Month 18}.
(c) Report on sterility testing as outlined in ANSI / AAMI / ISO 11135-1:2007 [Month 24].
(d) Deliver report on biocompatibility testing for sub-chronic (< 29-days) implantation as outlined in ANSI / AAMI / ISO 10993-3:2008 for the neural interfaces [Month 24].
(e) Report on electronics testing for sub-chronic (< 29-days) implantation as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Month 24].
(f) Report on surgical procedure validation via acute animal testing [Month 24].
(g) Validate and fully document a system that is ready for FDA IDE submission [Month 24].

3.1.15 IDE submission. The recipient shall present the design history file, fabrication data, and ANSI / AAMI / ISO data for sub-chronic (< 29 days) FDA IDE application.

3.1.15.1 The recipient shall support a pre-IDE meeting with the FDA to establish the system requirements, validation and verification data, and additional information required for the preparation and submission of IDE application [Months 23–24].

3.1.15.2 The recipient shall compile and write the master file for the FDA [Months 23–24].

3.1.15.3 The recipient shall produce the master file for FDA and the submit an IDE application for < 29-day human implantation of the system [Month 24].

Technical Area 3

The recipient shall perform basic research findings (b)(4) to inform the human stimulation studies in TA1 and guide device development in TA2.

The recipient shall document the protocols for measuring monkey (b)(4) memory (b)(4) and shall train animals in the (b)(4) task. In parallel, the recipient shall conduct studies of the neurophysiology of stimulation (b)(4)

The recipient shall then conduct behavioral studies of the electrophysiology (b)(4) in two monkeys. The recipient shall also perform a systematic study (b)(4) The recipient shall also probe the neurophysiology (b)(4)

3.1.16 Identifying neuronal basis of (b)(4) memory in NHPs and probing the role of stimulation (b)(4) This phase of the work seeks to characterize the patterns of neuronal activity that underlie (b)(4) memory in non-human primates. The recipient shall conduct (b)(4)

(b)(4) **recordings** (b)(4) .

3.1.16.1 The recipient shall design, program, and test experimental protocol for measuring monkey (b)(4) memory performance (b)(4) [Months 1-4].

(a) The recipient shall design and program a behavioral task for measuring monkey (b)(4) memory [Month 4].

3.1.16.2 The recipienst shall document the hardware interface for the (b)(4) task to interface with recording equipment (b)(4) [Months 3-5].

(a) The recipient shall document the hardware/software interface for interfacing electrophysiological recordings, eye tracker, and monkey behavioral paradigm [Month 5].

3.1.16.3 The recipient shall train (b)(4) to (b)(4) perform the (b)(4) memory task [Months 5-24].

(a) The recipient shall obtain 2 monkeys, complete pre-training health checks, place collars, complete quarantine and room acclimation procedures [Month 8].

(b) The recipient shall train monkeys in chairing and handling procedures, acclimate monkeys to working in the laboratory, begin food delay procedures, train monkeys on initial behavioral tasks, (b)(4) which will be used in the eye-tracking calibration procedure of the (b)(4) memory task [Month 10].

(c) The recipient shall train animals in the (b)(4) memory paradigm [Month 24].

3.1.16.4 The recipient shall prepare monkeys for recording and stimulation studies, including MRIs, surgeries to implant headposts and recording chambers, and craniotomies. The recipient shall conduct studies of neurophysiological correlates of monkey (b)(4) behavior without stimulation [Months 5-24] and shall:

(a) Perform pre-surgical MRIs on each monkey and perform surgeries to implant headposts. Complete recovery from surgery [Month 12].

(b) Train monkeys on initial joystick task, including eye calibration and fixation training with head fixation via headpost [Month 15].

(c) Train monkeys on the (b)(4) memory task, perform surgery to implant recording chamber [Month 18].

(d) Perform craniotomy and post-surgical MRI in both monkeys with contrast agent in chamber to determine location of recording targets [Month 20].

3.1.16.5 The recipient shall examine the dynamics (b)(4) in relation to task parameters [Months 20-24] and shall:

(a) Run animals in the (b)(4) memory task while recording neuronal activity (b)(4) [Month 24].

(b) Identify the patterns (b)(4) that encode (b)(4) during the task [Month 24].

3.1.17 Comprehensive examination of the electrophysiology of stimulation in non-human primates. (b)(4) **study of the electrophysiology of stimulation. The recipient shall perform a systematic study of the ability for** (b)(4) **stimulation** (b)(4) **and identify** (b)(4) **parameters** (b)(4) **. The recipient shall conduct both studies** (b)(4)

3.1.17.1 The recipient shall prepare untrained monkeys for (b)(4) recording and stimulation studies (b)(4) The recipient shall perform MRIs to guide electrode implantation, surgeries to implant headposts and recording chambers, and craniotomies.

(a) The recipient shall perform monkey surgeries to implant electrodes (b)(4) [Month 6].

3.1.17.2 The recipient shall demonstrate that neuronal stimulation (b)(4)

(a) The recipient shall show that (b)(4) stimulation (b)(4) Month 9].

(b) The recipient shall document results of data analyses (b)(4) [Month 11].

3.1.17.3 The recipient shall identify (b)(4) stimulation parameters.

(a) The recipient shall perform DBS studies in 3 additional animals and demonstrate the (b)(4) (b)(4) parameters (b)(4) across a range of animals [Month 12].

3.1.17.4 The recipient shall prepare 3 monkeys for (b)(4) recording and stimulation studies. (b)(4)

(a) The recipient shall analyze the ability of (b)(4) stimulation (b)(4) [Month 18].

3.1.17.5 The recipient shall conduct a systematic analysis of the (b)(4) parameters (b)(4) .

(a) The recipient shall characterize (b)(4) [Month 24].

3.2 OPTION PERIOD (PHASE II)

Technical Area 1

3.2.1 Extending computational model (b)(4)

3.2.1.1 The recipient shall extend the modeling framework (b)(4)

(a) The recipient shall extend behavioral models (b)(4) (b)(4) [Month 30].

3.2.1.2 The recipient shall document and publicly share a fully documented library of modeling functions (b)(4)

(a) The recipient shall open source a fully documented library (b)(4) [Month 48].

3.2.1.3 The recipient shall document software (b)(4) .

3.2.1.4 The recipient shall obtain ability (b)(4) . This effort will be informed by all of the data collected in Phase I of the project in both human and animal studies.

(a) The recipient shall develop software (b)(4) [Month 36].

3.2.1.5 The recipient shall (b)(4)

(a) The recipient shall ensure decumentation of more computationally efficient and user-friendly open-source analysis software (b)(4) [Month 48].

3.2.1.6 The recipient shall continue Electrophysiological recordings to define biomarkers of (b)(4) memory.

3.2.1.7 The recipient shall complete data collection in experiment FR1 and shall:

(a) Analyze data on an additional 9 patients from experiment FR1 [Month 30].
(b) Analyze data on an additional 18 patients from experiment FR1 [Month 36].
(c) Analyze data on an additional 27 patients from experiment FR1 [Month 42].
(d) Analyze data on an additional 36 patients from experiment FR1 [Month 48].
(e) Organize and annotate patient data from above experiment [Month 48].
(f) Complete final reports on data from the above. Analyses of final data to be completed within 6 months of project completion [Month 48].
(g) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(h) Fully document analysis functions; final version [Month 48].
(i) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(j) Provide final reporting on analyzed data from all patients run in the task in Phases 1–2 [Month 48].
(k) Post fully annotated data to the public data portal for all patients run in the task in Phases 1–2 [Month 48].

3.2.1.8 The recipient shall complete data collection in experiment CatFR1 and shall:

(a) Analyze data on an additional 11 patients from experiment CatFR1 [Month 30].
(b) Analyze data on an additional 22 patients from experiment CatFR1 [Month 36].
(c) Analyze data on an additional 33 patients from experiment CatFR1 [Month 42].
(d) Analyze data on an additional 45 patients from experiment CatFR1 [Month 48].
(e) Organize and annotate patient data from above experiment [Month 48].
(f) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(g) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(h) Fully document analysis functions; final version [Month 48].
(i) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(j) Provide final reporting on analyzed data from all patients run in the task in Phases 1–2 [Month 48].
(k) Post fully annotated data to the public data portal for all patients run in the task in Phases 1–2 [Month 48].

3.2.1.9 The recipient shall complete data collection in experiment YC1and shall:

(a) Analyze data on an additional 11 patients from experiment YC1 [Month 30].
(b) Analyze data on an additional 22 patients from experiment YC1 [Month 36].
(c) Analyze data on an additional 33 patients from experiment YC1 [Month 42].
(d) Analyze data on an additional 44 patients from experiment YC1 [Month 48].
(e) Organize and annotate patient data from above experiment [Month 48].
(f) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(g) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(h) Fully document analysis functions; final version [Month 48].
(i) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(j) Provide final reporting on analyzed data from all patients run in the task in Phases 1–2 [Month 48].
(k) Post fully annotated data to the public data portal for all patients run in the task in Phases 1–2 [Month 48].

3.2.1.10 The recipient shall complete data collection in experiment PAL1 and shall:

(a) Analyze data on an additional 5 patients from experiment PAL1 [Month 30].
(b) Analyze data on an additional 10 patients from experiment PAL1 [Month 36].
(c) Analyze data on an additional 15 patients from experiment PAL1 [Month 42].
(d) Analyze data on an additional 20 patients from experiment PAL1 [Month 48].
(e) Organize and annotate patient data from above experiment [Month 48].
(f) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(g) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(h) Fully document analysis functions; final version [Month 48].
(i) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(j) Provide final reporting on analyzed data from all patients run in the task in Phases 1–2 [Month 48].
(k) Post fully annotated data to the public data portal for all patients run in the task in Phases 1–2 [Month 48].

3.2.2 Stimulation to enhance (b)(4) memory

3.2.2.1 Design, program, pilot, execute, and analyze data from Experiment FR4. (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 26].
(b) Write initial data analysis scripts [Month 27].
(c) Analyze data on 4 patients from experiment FR4 [Month 33].
(d Analyze data on 8 patients from experiment FR4 [Month 38].
(e) Analyze data on 12 patients from experiment FR4 [Month 43].
(f) Analyze data on 16 patients from experiment FR4 [Month 48].
(g) Organize and annotate patient data from above experiment [Month 48].
(h) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(j) Fully document code for experiment [Month 26].
(k) Fully document analysis functions [Month 27].

(l) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.2 Design, program, pilot, execute, and analyze data from Experiment FR5. (b)(4)

The recipient shall
(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 1 patient from experiment FR5 [Month 33].
(e) Analyze data on 2 patients from experiment FR5 [Month 38].
(f) Analyze data on 3 patients from experiment FR5 [Month 43].
(g) Analyze data on 4 patients from experiment FR5 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.3 Design, program, pilot, execute, and analyze data from Experiment FR6. (b)(4)

The recipient shall:
(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyzed data on 4 patients from experiment FR6 [Month 33].
(e) Analyze data on 8 patients from experiment FR6 [Month 38].
(f) Analyze data on 12 patients from experiment FR6 [Month 43].
(g) Analyze data on 16 patients from experiment FR6 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.4 The recipient shall complete data collection in Experiment FR7 and shall:
(a) Analyze data on 1 additional patient from experiment FR7 [Month 30].

(b) Analyze data on an additional 2 patients from experiment FR7 [Month 36].
(c) Analyze data on an additional 4 patients from experiment FR7 [Month 42].
(d) Analyze data on an additional 6 patients from experiment FR7 [Month 48].
(e) Organize and annotate patient data from above experiment [Month 48].
(f) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(g) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(h) Fully document analysis functions; final version [Month 48].
(i) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(j) Provide final reporting on analyzed data from all patients run in the task in Phases 1–2 [Month 48].
(k) Post fully annotated data to the public data portal for all patients run in the task in Phases 1–2 [Month 48].

3.2.2.5 Design, program, pilot, execute, and analyze data from Experiment CatFR4 (n=12). (b)(4)

The recipient shall:
(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 3 patients from experiment CatFR3 [Month 33].
(e) Analyze data on 6 patients from experiment CatFR3 [Month 38].
(f) Analyze data on 9 patients from experiment CatFR3 [Month 43].
(g) Analyze data on 12 patients from experiment CatFR3 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.6 Design, program, pilot, execute, and analyze data from Experiment CatFR5 (n=4). (b)(4)

The recipient shall:
(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 1 patient from experiment CatFR5 [Month 33].
(e) Analyze data on 2 patients from experiment CatFR5 [Month 38].
(f) Analyze data on 3 patients from experiment CatFR5 [Month 43].
(g) Analyze data on 4 patients from experiment CatFR5 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of all data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].

(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Privide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.7 Design, program, pilot, execute, and analyze data from Experiment CatFR6 (n=12). (b)(4)

(b)(4)

The recipient shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 3 patients from experiment CatFR6 [Month 33].
(e) Analyze data on 6 patients from experiment CatFR6 [Month 38].
(f) Analyze data on 9 patients from experiment CatFR6 [Month 43].
(g) Analyze data on 12 patients from experiment CatFR6 [Month 48].
(h) Organize and annotate patient data from above [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully documentanalysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(d) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(e) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.8 Design, program, pilot, execute, and analyze data from Experiment CatFR7 (n=12). (b)(4)

The recipient shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 3 patients from experiment CatFR7 [Month 33].
(e) Analyze data on 6 patients from experiment CatFR7 [Month 38].
(f) Analyze data on 9 patients from experiment CatFR7 [Month 43].
(g) Analyze data on 12 patients from experiment CatFR7 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].

(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.9 Design, program, pilot, execute, and analyze data from Experiment CatFR8 (n=8). (b)(4) The recipient shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 2 patients from experiment CatFR8 [Month 33].
(e) Analyze data on 4 patients from experiment CatFR8 [Month 38].
(f) Analyze data on 6 patients from experiment CatFR8 [Month 43].
(g) Analyze data on 8 patients from experiment CatFR8 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.10 Design, program, pilot, execute, and analyze data from Experiment YC4 (n=22). (b)(4) The recipient shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 5 patients from experiment YC4 [Month 33].
(e) Analyze data on 10 patients from experiment YC4 [Month 38].
(f) Analyzed data on 16 patients from experiment YC4 [Month 43].
(g) Analyze data on 22 patients from experiment YC4 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.11 Design, program, pilot, execute, and analyze data from Experiment YC5 (n=22). The recipient (b)(4) shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 5 patients from experiment YC5 [Month 33].
(e) Analyzed data on 10 patients from experiment YC5 [Month 38].
(f) Analyze data on 16 patients from experiment YC5 [Month 43].
(g) Analyze data on 22 patients from experiment YC5 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.12 Design, program, pilot, execute, and analyze data from Experiment PAL4 (n=10. (b)(4) . The recipient shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 2 patients from experiment PAL4 [Month 33].
(e) Analyze data on 4 patients from experiment PAL4 [Month 38].
(f) Analyze data on 7 patients from experiment PAL4 [Month 43].
(g) Analyze data on 10 patients from experiment PAL4 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48]
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.13 Design, program, pilot, execute, and analyze data from Experiment PAL5 (n=10). (b)(4) The recipient shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 2 patients from experiment PAL5 [Month 33].
(e) Analyze data on 4 patients from experiment PAL5 [Month 38].

(f) Analyze data on 7 patients from experiment PAL5 [Month 43].
(g) Analyze data on 10 patients from experiment PAL5 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26)
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.14 Design, program, pilot, execute, and analyze data from Experiment DBS3 (n=34). Participants will perform a free recall task. (b)(4) The recipient shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [(Month 28].
(d) Analyze data on 8 patients from experiment DBS3 [Month 33].
(e) Analyze data on 16 patients from experiment DBS3 [Month 38].
(f) Analyze data on 25 patients from experiment DBS3 [Month 43].
(g) Analyzed data on 34 patients from experiment DBS3 [Month 48].
(h) Organize and annotate patient data from above [Month 48].
(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.15 Design, program, pilot, execute, and analyze data from Experiment DBS4 (n=34). (b)(4) . Participants will perform a free recall task. (b)(4) . The recipient (b)(4) shall:

(a) Design and program task [Month 26].
(b) Collect pilot data on normal controls [Month 28].
(c) Write initial data analysis scripts [Month 28].
(d) Analyze data on 8 patients from experiment DBS4 [Month 33].
(e) Analyze data on 16 patients from experiment DBS4 [Month 38].
(f) Analyze data on 25 patients from experiment DBS4 [Month 43].
(g) Analyze data on 34 patients from experiment DBS4 [Month 48].
(h) Organize and annotate patient data from above experiment [Month 48].

(i) Complete final reports on data from the above experiment. Analyses of final data shall be completed within 6 months of project completion [Month 48].
(j) Post all data collected so far in a deidentified format compatible with the public data portal [Month 48].
(k) Fully document code for experiment [Month 26].
(l) Fully document analysis functions [Month 27].
(m) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(n) Provide final reporting on analyzed data from all patients run in the task in Phase 2 [Month 48].
(o) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

Technical Area 2
Phase 2 objectives in TA2 shall be to support FDA IDE approval and clinical site training, develop clinical systems, and (b)(4) Phase 1 algorithms.

3.2.4 Update system architecture and individual components based on TA1. The recipient shall review and, if necessary, redefine, document and review the high-level system design requirements for the (b)(4) system based on the discovery and feedback from TA1 in phase 1.

3.2.4.1 The recipient shall review and, if necessary, redefine system level specification with TA1 team based on the phase 1 results [Months 25–30].

3.2.4.2 The recipient shall review and, if necessary, redefine the specifications for neural interfaces [Months 25–30].

3.2.4.3 The recipient shall review and, if necessary, redefine the specifications for electronics including the stimulating and recording electronics [Months 25–30].

3.2.4.4 The recipient shall review and, if necessary, redefine the sub-chronic safety and performance data required by the FDA for 29-day IDE approval [Months 25–30].

3.2.4.5 The receipient shall produce a final set of documents detailing the specifications for the overall system and its components [Month 30].

3.2.5 Fabrication of the (b)(4) stimulators for clinical studies. The recipient shall produce the balance of (b)(4) stimulator units for use at the clinical sites in early phase 2, to complete the total of one hundred units plus twenty backup units and shall:
(a) Produce forty tested and documented (b)(4) stimulators [Month 30].
(b) Produce an additional forty tested and documented (b)(4) stimulators [Month 36].

3.2.6 Manufacture and testing of human implantable system. The recipient shall build one hundred human quality systems for implantation in one hundred human patients, plus twenty backup systems. Systems shall use commercial neural interfaces, or OPTIONALLY (b)(4) arrays that are not yet available at this time.

3.2.6.1 The recipient shall assemble one hundred twenty five human quality systems for sub-chronic implantation in one hundred patients in an epilepsy monitoring unit [Months 25–36].

3.2.6.2 The recipient shall provide manufacturing documentation [Months 25–36].

3.2.6.3 The recipient shall sterilize the one hundred twenty systems for human implantation [Months 30–36] and shall:

(a) Complete sixty sterilized, human quality systems [Month 30].
(b) Complete an additional sixty sterilized, human quality systems [Month 36].

3.2.7 Algorithm prototyping system: (b)(4) algorithm development from TA1, Phase 1. The recipient shall document the development of a tool to (b)(4) successful TA1 algorithmsonto the (b)(4)

3.2.7.1 The recipient shall document the development of a (b)(4) tool to translate existing algorithms from phase 1 (b)(4) [Months 31–36].

3.2.7.2 The recipient shall document the development of a tool (b)(4) [Months 31–36].

3.2.7.3 The recipient shall ensure verification and validation testing and documentation for IDE submission [Months 35–36]. The recipient shall:

(a) Complete software tool (b)(4) [Month 36].
(b) Complete software tool for translating software algorithm (b)(4) [Month 36].

3.2.8 IDE submission for the (b)(4) algorithm from TA1. The recipient shall seek approval of update to FDA IDE for adding (b)(4) algorithm in the (b)(4) Stimulator.

3.2.8.1 The recipient shall submit the IDE to the FDA [Month 36].

3.2.8.2 The recipient shall obtain approval of IDE [Month 38].

3.2.9 Core project resources devoted to TA2: (b)(4) algorithms, computational cluster equipment and administration, integration between TA1, TA2, and TA3 modeling and electrophysiology shall be documented.

Technical Area 3

The recipient shall examine the ability of neuronal stimulation (b)(4) Furthermore, in non-behavioral studies the recipient shall design, test, and optimize a system (b)(4)

The recipient shall then run a third monkey in the behavioral studies with stimulation, allowing verification of priot results regarding the ability of stimulation to improve memory activity. The recipient shall examine the ability of stimulation (b)(4) to improve (b)(4) memory in NHPs. The recipient shall also continue to test and optimize the performance of a (b)(4) system (b)(4) using (b)(4) stimulation.

3.2.10 Identifying neuronal basis of (b)(4) memory in NHPs and probing the role of stimulation in modulating (b)(4) memory representations. (b)(4)

3.2.10.1 The recipient shall identify the patterns (b)(4) that correlate with successful (b)(4) memory and shall perform data analyses to identify (b)(4) signals associated with successful memory (b)(4) [Month 25].

3.2.10.2 The recipient shall document hardware and software design interface for stimulation of equipment [Months 25–27].

(a) The recipient shall document the design of a hardware and software interface (b)(4) [Month 27].

3.2.10.3 The recipient shall conduct studies (b)(4) [Months 28–31].

(a) The recipient shall run monkeys in the (b)(4) memory task (b)(4) [Month 31].

(b) The recipient shall show analyses (b)(4) [Month 31].

3.2.10.4 The recipient shall document software (b)(4) [Months 25–31].

(a) The recipient shall document (b)(4) Month 31].

3.2.10.5 The recipient shall conduct studies (b)(4) [Months 32-36].

(a) The recipient shall run Monkeys (b)(4) [Month 36].

3.2.10.6 The recipient shall analyze (b)(4) data from the (b)(4) memory task (b)(4) [Months 34-37].

(a) The recipient shall run data analyses (b)(4) [Month 37].

3.2.10.7 The recipient shall train a third monkey to use a joystick (b)(4) [Months 25–30].

(a) The recipient shall obtain third monkey, complete pre-training health checks, place collar, complete quarantine and room acclimation procedures [Month 27].

(b) The recipient shall train monkeys in chairing and handling procedures, acclimate monkeys to working in the laboratory, begin food delay procedures, train monkeys on initial behavioral tasks, (b)(4) [Month 30].

3.2.10.8 The recipient shall prepare third monkey for recording and stimulation studies, including MRIs, surgeries to implant headposts and recording chambers, and craniotomies. This monkey shall be used to explore other sites of potential stimulation [Months 33–44].

(a) The recipient shall perform pre-surgical MRIs on monkey and perform surgery to implant headposts. Complete recovery from surgery [Months 33-36].

(b) The recipient shall train monkeys on initial joystick task, including eye calibration and fixation training with head fixation via headpost [Month 39].

(c) The recipient shall train monkeys on the (b)(4) memory task, perform surgery to implant recording chamber [Month 42].
(d) The recipient shall perform craniotomy and post-surgical MRI in both monkeys with contrast agent in chamber to determine location of recording targets [Month 44].

3.2.10.9 The recipient shall conduct studies of (b)(4) stimulation in the third monkey, (b)(4) The recipient shall conduct studies of (b)(4) stimulation (b)(4) in the third monkey [Months 45–48].
(a) The recipient shall run third monkey in the (b)(4) memory paradigm (b)(4) and shall verify the results from earlier experiments in Monkeys 1 & 2 [Month 46].
(b) The recipient shall run third monkey in a new version of the (b)(4) memory paradigm while they receive (b)(4) stimulation (b)(4) [Month 48].

3.2.10.10 The recipient shall analyze behavioral and neuronal data from the (b)(4) memory (b)(4) (b)(4) [Months 47–48].
(a) The recipient shall show (b)(4) across the population of three monkeys compared with just one individual [Month 48].

3.2.11 Designing and optimizing a (b)(4) system (b)(4) The recipient shall design a (b)(4) system (b)(4).

3.2.11.1 The recipient shall design (b)(4) stimulation hardware and software system for using (b)(4) stimulation (b)(4).
(a) The recipient shall design of a (b)(4) system (b)(4) [Month 28].

3.2.11.2 The recipient shall prepare monkey for assessment of (b)(4) stimulation (b)(4) and perform MRIs to guide electrode implantation, surgeries to implant headposts and recording chambers, and craniotomies. The recipient shall:
(a) Document hardware/software interface design for chronic electrophysiological recording [Month 29].
(b) Train two animals on behavioral paradigm [Month 35].
(c) Perform MRIs to guide electrode implantation. Perform implantation surgeries [Month 36].
(d) Run animals on memory and non-memory tasks (b)(4) [Month 40].

3.2.11.3 The recipient shall compare the efficiency and reliability of (b)(4) system with existing (b)(4) systems and analyze the effects of (b)(4) stimulation on behavior. The recipient shall:
(a) Run (b)(4) stimulation with chronic implants [Month 42].
(b) (b)(4). [Month 45].
(c) Demonstrate the ability of (b)(4) stimulation (b)(4) [Month 48].

3.2.12 The recipient shall ensure experiment development and programming, computational cluster equipment and administration, integration between TA1, TA2, and TA3 modeling and electrophysiology.

3.3 PROGRAM MANAGEMENT AND REVIEW

The Government will actively monitor, review and approve the recipient's performance to ensure all the performers are in sync and matched with the Government's requirements. The Government will ensure that each of the performers share experimental data across the program and will further ensure that the performers develop techniques and capabilities that are compatible and integrate with each other. The recipient shall collaborate and cooperate with other performers in the program under the coordination of the Government team. At Government PI meetings, the recipient shall demonstrate technical capabilities and engage and/or challenge other performers in a cooperative and challenge environment. Along these lines, the Government will ensure that each performer shares technical information with the others to enable the testing/challenging of each other's capabilities. The Government will further oversee the program and will review, approve, and participate in the demonstrations.

3.3.1 Kick-off Meeting

The recipient shall hold a kick off meeting within 60 days of award of this agreement. In this meeting, the recipient shall present a program management plan and financial tracking plan.

3.3.2 Quarterly Financial Reports

The recipient shall provide quarterly financial progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to provide a brief project progress and inform the GTR and Program Manager of any potential issues.

3.3.3 Quarterly Technical Reporting

The recipient shall provide quarterly progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to present a summary of work completed by SOW tasking and milestones met, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work. Quarterly reports shall also include all technical data items generated including but not limited to experimental data, processed data along with methods of processing used, research reports and publications and software (source code and executables) .

3.3.4 Monthly Status Reports

The recipient shall provide monthly status reports which will include all relevant project data including, but not limited to, raw and analyzed electrophysiological signals as well as any necessary annotations and interpretations of the data, such as time-stamped patient behaviors, necessary for appropriate analyses and interpretation of the data. Patient data shall be provided in a coded format that protects patient identities but will contain diagnosis (signs/symptoms), interventions including system modifications, technical observations, diagnostic tests/results, and patient outcomes. In addition, information about the device delivering therapy including device serial numbers, device model numbers, date of event, and country/state of event shall be annotated with the data and therapy. This data shall be made available on database accessible across the program and to Government personnel.

3.3.5 Final Agreement Review

The recipient shall host a final agreement review. The purpose of this review is to present a summary of all work completed and milestones accomplished and to discuss any relevant future efforts similar to the contract, which may be pursued. This report shall be provided to the Government Technical Representative (GTR) and DARPA Program Manager. A final summary report shall be provided at the end of the program.

3.3.6 System Development Plan (SDP)

The recipient shall describe the scope of the design and development effort, describe hardware, software architectures and experimental procedures (as applicable) in sufficient detail for review and replication, reference any applicable documents and provide a schedule. The recipient shall share the SDP with the other program performers and the Government.

3.3.7 System Documentation
The recipient shall provide system documentation documenting the source code, protocol and algorithm analysis, hardware description, format specifications, system diagrams, part numbers, and any other data necessary to replicate and test the designs.

4.0 INCIDENTAL HARDWARE AND SOFTWARE
Hardware and software incidental to this research shall be made available to the Government.

5.0 REPORTS AND PRESENTATION MATERIALS
The reports and presentation materials shall be delivered as described in the data matrix.

6.0 TRAVEL
Long distance domestic travel is estimated for Program Review meetings and Conferences.

7.0 PLACE OF PERFORMANCE
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